seems to be the treatment of choice for severe hypotension or major dysrhythmias due to tricyclic antidepressant overdose. Bicarbonate therapy gives optimal results, but hyperventilation may also be effective. Phenytoin may well be another useful agent in this circumstance. It is theoretically advantageous because it does not increase atrioventricular block, and has been used successfully in one small series of mild overdoses. It has not yet been shown to work on patients with major overdose, however. Bicarbonate therapy to correct serum and cerebrospinal fluid acidosis, rather than to alkalinize the urine, is also extremely important in major salicylate overdose.

A number of other antidotes show significant promise. The use of pyridoxine may be critical in cases of significant isoniazid overdose, and folic acid may become a simple, safe, inexpensive and extraordinarily effective antidote for methanol and formaldehyde poisoning. Pyridoxine may work by preventing the decrease in brain γ-aminobutyric acid seen with isoniazid overdose; it has been associated with decreased incidence of seizures in small numbers of patients. Folate derivatives have been dramatically successful in experimental methanol and formaldehyde poisonings in animals. Formic acid produced by the metabolism of these drugs plays a major role in their toxicity, and folate significantly increases formate oxidation.

Naloxone hydrochloride, traditionally used for opiate overdoses, has been shown to have an effect on an increasing number of drugs. Of these, the most important is propoxyphene, for which naloxone should be given in doses about ten times those used for opiates. A variety of other agents, including ethanol and diazepam, have also been at least partially reversed in some experimental situations by the administration of naloxone, but the clinical significance of this is not clear.

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## Hyperbaric Emergencies

ALTHOUGH THE USE OF increased atmospheric pressure to treat disease has a colorful (and at times inglorious) history that dates back to 17th century England, only in the past 20 years has a scientific basis for hyperbaric oxygen therapy been derived. Most physicians, however, remain unfamiliar with the principles of and legitimate indications for hyperbaric oxygen therapy (HBOT). Emergency physicians have a particular need to know about this therapy because many hyperbaric emergencies present via emergency departments.

Five mechanisms of action of hyperbaric oxygen therapy are currently recognized: (1) the mechanical effect of increased pressure, (2) the mass action effect of pure oxygen at increased pressure, (3) the vasoconstrictor effect of hyperbaric oxygen, (4) direct and indirect antibiotic effects and (5) enhancement of wound healing (applicable to compromised wounds only). In general, more than one of these effects are useful in a given condition. In no case does hyperbaric oxygen therapy supplant standard medical and surgical treatment; it is always adjunctive.

The Undersea Medical Society has issued a report on hyperbaric oxygen therapy that groups conditions that have been treated with hyperbaric oxygen into one of four categories according to the apparent efficacy of such treatment. Category I disorders are those for which hyperbaric oxygen therapy is the primary method of treatment (for example, decompression sickness and diving air embolism) or for which the efficacy of adjunctive hyperbaric oxygen therapy has been amply shown by research and clinical experience. Among the acute nondiving-related category I conditions are carbon monoxide poisoning, cyanide poisoning, smoke inhalation with presumptive carbon monoxide or cyanide poisoning, iatrogenic or traumatic air embolism, gas gangrene, mixed aerobic and anaerobic infections causing tissue necrosis, and cases of exceptional blood loss or life-threatening anemia when blood transfusion is impossible or delayed.

Category II disorders are those for which data from animal studies or from clinical experience indicate a beneficial role for adjunctive hyperbaric oxygen therapy but for which the data are limited. Emergency conditions included in category II are acute peripheral arterial insufficiency (due to any number of causes), crush injury, head and spinal cord trauma (but only if HBOT can be started within four hours of injury), retinal artery insufficiency and thermal burns. Some investigators have also found hyperbaric oxygen therapy to be a useful surgical adjunct in reimplantations, vascular and cardiac operations, scleral buckling procedures and surgical procedures in severely ill patients.

Category III disorders are those for which clinical data are very limited or only theoretical reasons suggest a possible beneficial role for hyperbaric oxygen therapy. HBOT must be viewed as investigational only in these conditions. Acute conditions included in category III are poisoning from hydrogen sulfide or carbon tetrachloride, ergotism, frostbite, musculoskeletal compartment syndromes, acute cerebrovascular accidents, migraine and cluster headaches, acute mesenteric thrombosis, sickle cell crisis and pneumatosis cystoides intestinalis.

Category IV disorders are ones for which there is no rational basis for using hyperbaric oxygen therapy. These include arthritis and other degenerative problems, hypertension and loss of hair color or sexual vitality. Regrettably, hyperbaric oxygen is occasionally being used to treat these kinds of conditions, but such practice should be strongly discouraged.

Hyperbaric oxygen therapy was once an exotic treatment confined to very few centers, but the development

of less expensive and less complicated monoplace hyperbaric chambers, increasing evidence of the benefits of this form of therapy and the expansion of the recreational and commercial diving industries have led to the proliferation of hyperbaric treatment facilities in recent years. Because many of the established indications for this treatment will be seen first in an emergency department, emergency and other acute care physicians should be familiar with the principles of hyperbaric medicine and should maintain a close liaison with local and regional hyperbaric treatment facilities.

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## Naloxone—New Uses?

THE ENDOGENOUS OPIATE β-endorphin is stored in the anterior pituitary gland along with adrenocorticotropic hormone (ACTH), and in situations of acute stress both ACTH and β-endorphin are released. Endogenous opiates, like exogenous opiates, have been shown to produce hypotension and bradyarrhythmias; it has been suggested that endorphin release may contribute to the hypotension associated with a variety of shock states in humans.

Naloxone hydrochloride (Narcan) is a narcotic antagonist without independent agonist properties. It is approved by the Food and Drug Administration for treatment of narcotic drug overdose, narcotic depression of newborn infants and reversal of narcotic analgesia. Naloxone works by selectively competing with narcotic agonists for specific opiate receptor sites in the central nervous system. All the apparent physiologic effects of naloxone in a narcotized patient—mydriasis, piloerection, agitation, respiratory stimulation and hypertension—are due to reversal of narcotic effects. Naloxone has been proved to be extremely safe and effective for its approved uses. With the discoveries of β-endorphin, as well as β-enkephalin and specific opiate receptors in the central nervous system, and the observations regarding the physiologic effects of endorphin noted above, new applications for naloxone, particularly in shock states, have been considered.

In 1978 Holaday and Faden showed naloxone-mediated reversal of endotoxin-induced hypotension in rats. Similar salutary effects have been reported in a variety of experimental studies of hemorrhagic shock in animals. Naloxone treatment has also been shown to protect against shock in cats with spinal cord injury and is associated with improved neurologic recovery in these animals. Preliminary observations in patients with septic or cardiogenic shock refractory to conventional fluid and pressor therapy indicate that naloxone therapy can have a beneficial effect on systemic arterial pressure, cardiac output and mental status. Very large doses (up to 8 mg) have been used and the degree of improvement in blood pressure response has been highly variable. Although these studies are encouraging, they are preliminary in nature and the use of naloxone in shock remains entirely experimental.

Several anecdotal reports suggest a possible future role for naloxone administration in the reversal of alcohol- and diazepam-induced central nervous system depression, as well as correction of hypotension and apnea in clonidine poisoning. The mechanism of action is not established in these cases, but may again be related to reversal of a still undefined endorphin-mediated phenomenon.

The effectiveness of the use of naloxone in cases of clonidine overdose is provocative. Clonidine administration has been reported to be effective in treating symptoms of narcotic withdrawal, presumably by antagonizing specific autonomic effects. The usefulness of naloxone in treating clonidine overdose suggests that clonidine may itself stimulate endogenous β-endorphin production.

With naloxone, a drug that for the past ten years has been used with great effectiveness in a small number of clinical situations, we appear to be on the verge of a wide variety of valuable and exciting new applications. Further studies are needed to define appropriate doses, effects and possible complications.

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## Poisoning With the New Antidepressant Maprotiline

MAPROTILINE HYDROCHLORIDE (LUDIOMIL) is a tetracyclic antidepressant now available in this country after extensive use in Europe. As its use and sales increase in this country, emergency physicians can expect to see more patients with maprotiline side effects and overdoses.

Maprotiline has a half-life of between 27 and 58 hours in normal volunteers given therapeutic doses. It is 88 percent protein bound and has an enormous apparent volume of distribution (22.6 liters per kg of body weight).

In therapeutic doses, side effects of drowsiness, dry mouth, hypotension, tachycardia and incomplete heart block occur with an incidence similar to those of the tricyclic antidepressants, but there is a pronounced increase in the incidence of seizures.

Maprotiline overdose also differs from overdose with tricyclic antidepressants in the incidence of drug-induced seizures. As many as 25 percent to 50 percent of adult patients overdosing on maprotiline have seizures, compared with a 6 percent incidence reported with tricyclic antidepressants. Other symptoms seen with maprotiline overdose in approximate order of frequency